

substrate surface, (ii) the DNA sequences are purified polynucleotides, and (iii) the DNA sequences are non-covalently bound to a polycationic polymer on the surface of the substrate --.

-- 37. The substrate according to claim 36, wherein the DNA sequences are cDNAs --.

REMARKS

The title has been amended to make it more descriptive of the claimed invention. The specification has been amended to reflect that the United States government may have certain rights in the present invention. The specification has been amended to reflect that this application is a continuation of application Serial No. 08/688,488, and to update the status of the great grandparent and great-great-grandparent applications. The specification has been amended to correct various typographical and syntax errors. It is apparent that no new matter was added by any of these amendments and they require no further comment.

Applicants have amended the specification to describe the present invention with greater particularity. Specifically, Applicants have amended the specification explicitly to recite that the present microarray invention includes microarrays having a density of at least about 400 per cm², corresponding to typical diameters of about 250 μm for regions in the microarray. Support for these amendments to the specification is found, among other places, in priority application Serial Nos. 08/261,388 (great-great-grandparent) and 08/477,809 (great-grandparent), which were incorporated by reference in the present application as filed at page 1, lines 4-15. For example, the great-great-grandparent application recites at page 8, lines 7-11, that each region in the microarray may be "about 25-250 μm, and are separated from other regions in the array by about the same

distance” (emphasis added). Similarly, the great-grandparent application recites at page 12, lines 5-9, that each region in the microarray may be “about 10-250 μm , and are separated from other regions in the array by about the same distance” (emphasis added). It follows that a microarray having regions of 250 μm in diameter, spaced apart from one another by about the same distance (i.e., 250 μm) necessarily has 20 microarray positions per cm, which is about 400 regions per cm^2 . This density is recited in claims 7 and 34. These same amendments were made in parent application Serial No.08/688,488; they do not constitute new matter.

Claims 1-6 have been canceled without prejudice. Claims 7-37 have been added, to point out Applicants’ invention with greater clarity and particularity.

Claims 7-35 correspond to claims 7-35 of parent application Serial No. 08/688,488, except that the word “essentially” has been deleted from claims 7 and 34. The support for those claims is set out in Applicants’ Response To Office Action dated April 20, 1998 in the parent application. Applicants additionally note the following support.

With respect to the limitation that there be “400 or more regions” in the microarray, Applicants respectfully refer the Examiner to page 32, lines 15-20 of the specification, which states that in a “general embodiment” of the invention, the microarray is created by arraying the DNA sequences in “1.0 cm^2 ”. *See also* page 42, lines 1-5. Applicants submit that these disclosures, of a 1.0 cm^2 microarray, considered in light of the disclosure discussed above that the microarray may have a density of 400 or more regions per cm^2 , supports the instant limitation that the arrays have 400 or more regions.

With respect to the limitation in claim 35 regarding detection of a two-fold change in polynucleotide abundance, Applicants refer the Examiner to page 8, lines 13-19, and page 26, lines 20-23 of the application as filed.

New claim 36 is directed to a particular embodiment of Applicants' invention wherein (1) the microarray has a density of 400 or more regions per cm² of substrate surface, (2) the DNA sequences at each region of the microarray are purified polynucleotides and (3) the DNA sequences are non-covalently bound to a polycationic polymer on the surface of the substrate. The support for the density limitation is as described by Applicants for claim 7. The support for the non-covalent binding to a polycationic polymer is the same as for claims 15 and 16. *See, e.g.*, page 13, lines 15-23, of the specification. The support for the DNA sequences being purified polynucleotides is found at, among other places, page 9, line 21 to page 10, line 9 and page 14, line 17 to page 15, line 14. By the term "purified DNA sequences", Applicants mean that the DNA sequences are not present in a cell. New dependent claim 37 is supported, for example, by the disclosure at page 15, lines 3-7.

Applicants note that an Information Disclosure Statement is being filed concurrently with this Preliminary Amendment. In addition, Applicants wish to apprise the Examiner of three related, pending applications, in addition to priority application Serial Nos. 08/261,388, 08/477,809 (now U.S.P. 5,807,522), 08/514,875, and 08/688,488. These are: (1) Serial No. 09/001,027, a continuation application of great-grandparent Serial No. 08/477,809, (2) an application filed November 19, 1998, Serial No. not yet assigned, which is a continuation of

application Serial No. 09/001,027, and (3) an application filed November 10, 1998, Serial No. not yet assigned, which is a continuation of grandparent Serial No. 08/514,875.

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In view of the foregoing, entry of the amendments and allowance of the claims is respectfully requested. The Examiner is invited to contact the undersigned attorney at (650) 614-4654 with any questions, comments or suggestions relating to the above-identified patent application.

Respectfully submitted,



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